

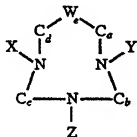
Amendments to the Claims:

The listing of claims will replace all prior versions and listings of claims in the application:

Listing of the Claims

1.-13. Canceled

14. (Withdrawn, currently amended) A method for downregulating CD4 expression on of T cells by exposing the T cells to ~~an amount~~ of a triaza compound of formula:



or a pharmaceutically acceptable salt or solvate thereof in an amount that is effective for downregulating expression of CD4₁ wherein:

W represents a bridge carbon which is unsubstituted or which is bonded directly or indirectly to one or two polar or non-polar side group substituents selected from the group consisting of double-bonded carbon (=C(H)₂ or =C(R)₂), double bonded oxygen (=O), hydroxyl, alkyl of about one to 10 carbons alkenyl of about two to 10 carbons (~~preferably of 2 to 6 carbon atoms~~); a substituted alkyl group carrying a charged substituent, ~~such as an~~ S(R'')₂⁺, ~~an~~ N(R'')₃⁺, a PR₃⁺, or an OSO₃⁻ group, alkoxy of about one to 10 carbons; aryl of about 6 to 12 carbons; halogen, methyl halogen (-CT₃, -CHT₂, or -CH₂T), methylene halide (=CT₂); optionally substituted epoxide (~~or oxirane~~); acyl (-CO-R); (-CO₂-R); CH₂OH and

hydrogen; where halogen is F, Cl, I or Br; T, independently of other T, is F, Cl, I or Br, but preferably all T are the same halogen; R, independently of other R, is an optionally substituted alkyl of about one to 10 carbons (preferably of one to 6 carbon atoms), an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons and R" is a hydrogen or an alkyl group having from one to 10 carbon atoms and W may be bonded to one hydrogen and one polar or non-polar group;

X and Y independently represent an optionally substituted aryl group (Ar), an optionally substituted alkyl group having from one to 10 carbon atoms, or an optionally substituted alkenyl group having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L; where the linker group L can be is selected from sulfonyl ($-\text{SO}_2-$), $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy ($-\text{OCO}-$), carbonyl ($-\text{CO}-$), or alkyl (e.g., $(\text{CH}_2)_n$, where n is 1 or 2-; where Ar comprises at least one aromatic homocyclic or heterocyclic ring having from five to seven members; ~~wherein the Ar ring can be~~ is optionally substituted with one or more non-hydrogen substituent groups; ~~wherein Ar group~~ optional substituents include one or more halogens, one or more $-\text{CN}$; one or more $-\text{SO}_3$, $-\text{SH}$, $-\text{SR}$ or $-\text{S-OR}$ groups; one or more trihalomethyl groups; one or more NO , one or more NO_2 , one or more NH_2 , NHR or $\text{N}(\text{R})_2$ groups; one or more alkyl groups, one or more alkoxy groups, one or more hydroxyl groups, one or more acyl groups ($-\text{COH}$ or $-\text{CO-R}$), one or more acid or ester groups ($-\text{CO}_2\text{H}$ or $-\text{CO}_2\text{R}$, respectively), where R, independently of other R, is an alkyl of about one to 10 carbons or an aryl group of about 7 to 10 carbons and wherein X and Y are not both an alkyl group;

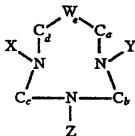
Z represents a hydrogen, or optionally substituted aryl, alkyl or alkenyl groups attached to the triaza macrocycle through an optional linking group L^3 , wherein the aryl, alkyl and alkenyl groups and the linking group of L^3 are as described under defined for X and Y variables above;

C labeled with subscripts a-d in formula I represent carbon bridges, preferably alkylene bridges, between nitrogens, ~~these carbon bridges~~, the length lengths of which is are defined by the values of subscripts a-d and e, the carbon bridges may all be the same length or may differ in length, each bridge may be composed entirely of saturated alkyl groups, or one or more bridges may contain one or more double or triple bonds between carbons, ~~additionally~~ one or more bridge carbons ~~can be~~ are optionally substituted with one or more polar groups, ~~for example, halogens or hydroxy groups~~, and ~~additionally~~ aromatic, non-aromatic rings or both may be fused to one or more of the carbon atom bridges; and

a and d, independently, represent a number from zero to 10; b and c, independently, represent a number from one to 10; and e represents a number from zero to three.

15.-23. Canceled

24. (Withdrawn, currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective ~~combined~~ amount or combined amount of one or more triaza macrocycle compounds of formula:



or a pharmaceutically acceptable salt or solvate thereof that is effective for downregulating expression of CD4 wherein:

W represents a bridge carbon which is unsubstituted or which is bonded directly or indirectly to one or two polar or non-polar side group substituents selected from the group consisting of double-bonded carbon ($=C(H)_2$ or $=C(R)_2$), double bonded oxygen ($=O$), hydroxyl, alkyl of about one to 10 carbons, alkenyl of about two to 10 carbons (preferably of 2 to 6 carbon atoms); a-substituted alkyl group carrying a charged substituent, such as an $-S(R'')_2^+$, an $-N(R'')_3^+$, a $-PR_3^+$, or an $-OSO_3^-$ group, alkoxy of about one to 10 carbons; aryl of about 6 to 12 carbons; halogen, methyl halogen ($-CT_3$, $-CHT_2$, or $-CH_2T$), methylene halide ($=CT_2$); optionally substituted epoxide (or oxirane); acyl ($-CO-R$); ($-CO_2-R$); CH_2OH and hydrogen; where halogen is F, Cl, I or Br; T, independently of other T, is F, Cl, I or Br, but preferably all T are the same halogen; R, independently of other R, is an optionally substituted alkyl of about one to 10 carbons (preferably of one to 6 carbon atoms), an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons and R'' is a hydrogen or an alkyl group having from one to 10 carbon atoms and W may be bonded to one hydrogen and one polar or non-polar group;

X and Y independently represent an optionally substituted aryl group (Ar), an optionally substituted alkyl group having from one to 10 carbon atoms, or an optionally substituted alkenyl group having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L; where the linker group L can be is selected from sulfonyl ($-SO_2-$), $-SO-$, $-PO-$, $-PO(OH)-$, $-PO(H)-$, $-PO_2(OH)-$, $-PO_2(H)-$, $-PO_3(OH)-$, carboxy ($-OCO-$), carbonyl ($-CO-$), or alkyl (e.g., $(CH_2)_n$ where n is 1 or 2; where Ar comprises at least one aromatic homocyclic or heterocyclic ring having from five to seven members; wherein the Ar ring can be substituted with one or more non-hydrogen substituent groups; where Ar-group optional substituents include one or more halogens, one or more $-CN$; one or more $-SO_3$, $-SH$, $-SR$ or $-S-OR$ groups; one or more trihalomethyl groups; one or more NO , one or more NO_2 , one or more NH_2 , NHR or $N(R)_2$ groups; one or more alkyl groups, one or more alkoxy groups, one or more

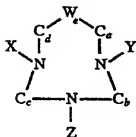
hydroxyl groups, one or more acyl groups (-COH or -CO-R), one or more acid or ester groups (-CO₂H or -CO₂R, respectively), where and R, independently of other R, is an alkyl of about one to 10 carbons or an aryl group of about 7 to 10 carbons and wherein X and Y are not both an alkyl group; Z represents a hydrogen, or optionally substituted aryl, alkyl or alkenyl groups attached to the triaza macrocycle through a optional linking group L³, wherein the aryl, alkyl and alkenyl groups and ~~the linking group of Z~~ L³ are as described under defined for X and Y variables above;

C labeled with subscripts a-d represent carbon bridges, ~~preferably alkylene bridges, between nitrogens, these carbon bridges,~~ the length lengths of which is are defined by the values of subscripts a-d and e, the carbon bridges may all be the same length or may differ in length, each bridges may be composed entirely of saturated alkyl groups, or one or more bridges may contain one or more double or triple bonds between carbons, ~~additionally~~ one or more bridge carbons can be optionally substituted with one or more polar groups, ~~for example, halogens or hydroxy groups,~~ and ~~additionally~~ aromatic, non-aromatic rings or both may be fused to one or more of the carbon atom bridges; and

a and d, independently, represent a number from zero to 10; b and c, independently, represent a number from one to 10; and e represents a number from zero to three.

25.-28. Canceled

29. (New) A method for treating an individual suffering from a pathological conditions which is ameliorated by suppression of CD4+-T-cell-mediated immune response, other than a condition resulting from viral infection, which comprises the steps of administering to the individual a therapeutically effective amount or combined amount of one or more triaza macrocyclic compounds having the formula:



or a

pharmaceutically
acceptable salt or solvate

thereof, that is effective for downregulating expression of CD4,

wherein:

W represents a bridge carbon which is unsubstituted or which is bonded directly or indirectly to one or two polar or non-polar side group substituents selected from the group of double-bonded carbon ($=C(H)_2$ or $=C(R)_2$), double bonded oxygen ($=O$), hydroxyl, alkyl of one to 10 carbons, alkenyl of two to 10 carbons, a substituted alkyl group carrying a charged substituent, alkoxy of one to 10 carbons, aryl of 6 to 12 carbons, halogen, methyl halogen, methylene halide, optionally substituted epoxide, $-COR$ group, $-CO_2R$, CH_2OH or hydrogen; where R, independently of other R, is an optionally substituted alkyl of one to 10 carbons, an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons and W may be bonded to one hydrogen and one polar or non-polar group;

X and Y, independently, represent an optionally substituted aryl (Ar), an optionally substituted alkyl having from one to 10 carbon atoms, or an optionally substituted alkenyl having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L, where the linker group L is selected from sulfonyl ($-SO_2-$), $-SO-$, $-PO-$, $-PO(OH)-$, $-PO(H)-$, $-PO_2(OH)-$, $-PO_2(H)-$, $-PO_3(OH)-$, carboxy ($-OCO-$), carbonyl ($-CO-$), or alkyl, where Ar comprises at least one aromatic homocyclic or heterocyclic ring having from five to seven members and wherein X and Y are not both alkyl groups;

Z represents a hydrogen, or optionally substituted aryl, alkyl or alkenyl groups attached to the triaza macrocycle through optional linking group L^3 , wherein the aryl, alkyl and alkenyl groups are as defined for X and Y variables above and L^3 is as defined for L above;

Optional substitution includes substitution with one or more non-hydrogen substituent groups selected from halogens, $-CN$, $-SO_3$, $-SH$, $-SR$, $-S-OR$, trihalomethyl, NO , NO_2 , NH_2 , NHR , $N(R)_2$, alkyl, alkoxy, hydroxyl, $-COH$, $-CO-R$, $-CO_2H$ or $-CO_2R$ groups, where R, independently of other R, is an alkyl of one to 10 carbons or an aryl group of 6 to 12 carbons;

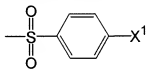
C labeled with subscripts a-d represent carbon bridges between nitrogens, the length of which is defined by the values of subscripts a-d and e, the carbon bridges may all be the same length or may differ in length, and each carbon bridge may be composed entirely of saturated alkyl groups, or one or more bridges may contain one or more double or triple bonds between carbons, one or more bridge carbons are optionally substituted with one or more polar groups and aromatic, non-aromatic rings or both are optionally fused to one or more of the carbon atom bridges; and

a and d, independently, represent a number from zero to 10; b and c, independently, represent a number from one to 10; and e represents a number from zero to three.

30. (New) The method of claim 29 wherein e is 1 and W is double-bonded carbon ($=C(H)_2$ or $=C(R)_2$), a double bonded oxygen ($=O$), or a methylene halide, where R independently of other R, is an optionally substituted alkyl of about one to 10 carbons, an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons.
31. (New) The method of claim 29 wherein X and Y, independently, are optionally substituted aryl groups attached to the triaza macrocycle through an optional

linker group L selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, $-\text{OCO}-$, $-\text{CO}-$, or alkyl.

32. (New) The method of claim 31 wherein L is $-\text{SO}_2-$.
33. (New) The method of 32 wherein X and Y are selected from tosyl groups, dansyl groups or analogues thereof.
34. (New) The method of claim 29 wherein X and Y groups have the structure:

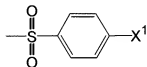


where X^1 is a group selected from a halogen, $-\text{CN}$, $-\text{SO}_3$, $-\text{SH}$, $-\text{SR}$, $-\text{S-OR}$, trihalomethyl, $-\text{NO}$, $-\text{NO}_2$, $-\text{NH}_2$, $-\text{NHR}$, $-\text{N(R)}_2$, alkyl, alkoxy, hydroxyl, $-\text{COH}$, $-\text{COR}$, $-\text{CO}_2\text{H}$, or $-\text{CO}_2\text{R}$.

35. (New) The method of claim 29 wherein Z is an optionally substituted aryl, alkyl or alkenyl group optionally attached to the triaza macrocycle through a linking group L^3 selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, $-\text{OCO}-$, $-\text{CO}-$, or alkyl.
36. (New) The method of claim 29 wherein Z is an optionally substituted aryl, alkyl or alkenyl group directly attached to the triaza macrocycle.
37. (New) The method of claim 29 wherein Z is a benzyl group.
38. (New) The method of claim 29 wherein Z is a benzyl group, a methylene cyclohexane group or a methylene cyclohexene group.
39. (New) The method of claim 29 wherein a, d and e are all 1 and b and c are 3.

40. (New) The method of claim 29 wherein e is 1 and W is $>C=C(H)_2$.

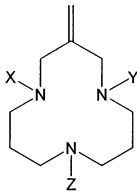
41. (New) The method of claim 29 wherein X and Y have the structure:



where X^1 is a group selected from a halogen, -CN, -SO₃, -SH, -SR, -S-OR, trihalomethyl, -NO, -NO₂, -NH₂, -NHR, -N(R)₂, alkyl, alkoxy, hydroxyl, -COH, -COR, -CO₂H, or -CO₂R.

42. (New) The method of claim 41 wherein X^1 is an alkyl, alkoxy or hydroxyl group.

43. (New) The method of claim 29 wherein the one or more triaza macrocyclic compounds have the formula:



wherein X, Y and Z, independently, are optionally substituted aryl groups, optionally substituted alkyl groups having from one to 10 carbon atoms, or optionally substituted alkenyl groups having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L selected from -SO₂ -, -SO -, -PO -, -PO(OH) -, -PO(H) -, -PO₂(OH) -, -PO₂(H) -, -PO₃(OH) -, carboxy (-OCO-), carbonyl (-CO-), or (CH₂)_n, where n is 1 or 2, and wherein X and Y are not both an alkyl group.

44. (New) The method of claim 43 wherein Z is a benzyl group directly bonded to N.

45. (New) The method of claim 43 wherein X and Y are both optionally substituted aryl groups linked to the triaza macrocycle through linker group L which is selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy ($-\text{OCO}-$), carbonyl ($-\text{CO}-$), or $(\text{CH}_2)_n$, where n is 1 or 2.
46. (New) The method of claim 43 wherein X and Y are both optionally substituted aryl groups linked to the triaza macrocycle through linker group $-\text{SO}_2$.
47. (New) The method of claim 43 wherein X and Y are both optionally substituted phenyl groups linked to the triaza macrocycle through linker group $-\text{SO}_2$.
48. (New) The method of claim 43 wherein X and Y are phenyl groups substituted with one or more alkyl groups, alkoxy groups, $-\text{NO}_2$ groups, $-\text{NH}_2$ groups, or halides.
49. (New) The method of claim 48 wherein X and Y are para-substituted phenyl groups.
50. (New) The method of claim 48 wherein X and Y are para-substituted phenyl groups wherein the para-substituents are alkyl groups or alkoxy groups.
51. (New) The method of claim 43 wherein X and Y are optionally substituted phenyl groups optionally linked to the linked to the triaza macrocycle through linker group L which is selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy ($-\text{OCO}-$), carbonyl ($-\text{CO}-$), or $(\text{CH}_2)_n$, where n is 1 or 2.
52. (New) The method of claim 51 wherein Z is an optionally substituted phenyl group optionally linked to the linked to the triaza macrocycle through linker group

L which is selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO}(\text{OH})-$, $-\text{PO}(\text{H})-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy ($-\text{OCO}-$), carbonyl ($-\text{CO}-$), or $(\text{CH}_2)_n$, where n is 1 or 2.

- 53. (New) The method of claim 52 wherein X and Y are optionally substituted phenyl groups linked to the linked to the triaza macrocycle through $-\text{SO}_2-$.
- 54. (New) The method of claim 53 wherein Z is a benzyl group.
- 55. (New) The method of claim 54 wherein X and Y are para-substituted phenyl groups.
- 56. (New) The method of claim 55 wherein X and Y are para-substituted phenyl groups wherein the para-substituent is an alkoxy group or an alkyl group.
- 57. (New) The method of claim 55 wherein the para-substituent is a methoxy group or a methyl group.
- 58. (New) The method of claim 29 wherein the pathological condition is an autoimmune disorder or a chronic inflammatory disease.
- 59. (New) The method of claim 29 wherein the pathological condition is graft-versus host disease or transplant rejection.
- 60. (New) The method of claim 29 wherein the pathologic condition is rheumatoid arthritis, type I-diabetes mellitus, autoimmune demyelinating diseases such as multiple sclerosis, inflammatory bowel disease syndrome, psoriasis, discoid lupus erythematosus, systemic lupus erythematosus (SLE), adult respiratory distress syndrome, cardiovascular atherosclerosis, leukocytosis, or asthma.